

Transferring Research Knowledge to Public Policy

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By

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Abstract

Each year, billions of tax dollars are spent on basic discovery, intervention development, and efficacy research in the United States. Meanwhile, hundreds of billions of tax dollars are spent on health service delivery programs. Unfortunately limited funds are spent to gain knowledge on how to best ensure that the lessons learned from basic science informs and improves the quality of health services and the availability of evidence-based approaches. In order to close this discovery-delivery gap, researchers and their funding agencies must not only recognize the gap between basic discovery and intervention development, but they must work together with practitioners and their funding agencies to recognize and implement advances. There continues to be a growing gap between innovative interventions developed through research and the ability to actually deliver and have impact of improving public health.

A thorough review of the literature on translational research or knowledge translation followed by its application to an ongoing international collaborative program will be presented.

❖ Introduction

The National Institute of Health (NIH) has an investment budget of \$28 billion for medical research. \$23.6 billion is allocated to research funding provided to 212,000 researchers through 48,000 awarded grants at more than 3,000 institutions. This funding is allocated for the more than 40,000 funding applications submitted to the NIH each year (AAMC, 2004).

A recent report released regarding the state of the U.S. economy by The Organization for Economic Cooperation and Development (OECD) warns the U.S. is headed for a budget crisis unless it reforms healthcare spending (OECD., 2007). Without drastic reform, the report forecasts healthcare costs will consume approximately 20% of Gross Domestic Product (GDP)

by 2050 (Jessen, 2007). Coincidentally, the federal investment in basic and applied research, which has consistently declined since 2004, is projected to continue the trend in 2009 the fifth year in a row (AAAS, 2008). Even more perturbing, there is every indication that funding for new Clinical and Translational Science (CTS) entities, the mean by which U.S. science is mandated to break the growing barriers between clinical and basic research will continue to be poorly supported in the current economic crisis (AAAS, 2008).

This information should represent a serious alarm. It seems incredibly obvious we must improve the efficiency and effectiveness in the way we practice medicine, perform research and deliver results to the public. In regards to the later, there is an urgent need to close a widening gap between basic research and clinical practice to reduce costs while improving the efficiency of the processes that ultimately leading to better health care for our communities. Although we have reduced the abysmal gap that initially took the British Navy from the 17th century 264 years to move from research (identifying citric juice as prevention for scurvy) to practice (carrying citrus juice on board), we have yet to understand the processes and effects of moving evidence-based interventions to communities. A more recent illustration comes from the results obtained from basic clinical research consistently showing marked benefits of early intervention (percutaneous trans-luminal coronary angioplasty or PTCA) to achieve reperfusion in patients with acute myocardial infarction. Guidelines developed in 1996 by the American College of Cardiology and the American Heart Association advocated rapid treatment with PTCA or fibrinolysis, with the former being preferentially recommended (Lenfant, 2003a). Data from the National Registry of Myocardial Infarction showed that in the last quarter of 2002, nearly one third of all patients nationwide who presented with an acute myocardial infarction and who were eligible for reperfusion received neither of these therapies (NRMI, 2002). Unfortunately there are

many more examples like these. It is safe to say that we still have an astonishing 15 to 20 year lag in moving basic clinical research to clinical practice.

Another profound example comes from Lee Nadler's (Senior VP for Experimental Medicine at the Dana Farber Cancer Institute in Boston, who is in charge of promoting the translation of basic research discoveries into clinical applications) comments when invited to give the Seventh Joseph H. Burchenal Clinical Research Award Lecture at the American Association of Cancer Research in April of 2002. He caused grave consternation among the audience who had expected to hear a scientific lecture and instead received a warning that physician-scientists would "go the way of the dinosaur" if the community did not invest more seriously in translational research. Nadler further advised that translational research should be based around teams rather than individuals, stating "Virtually nobody is attempting to create the necessary middle [infrastructure] that takes work from the lab to the clinic" (Birmingham, 2002). What Nadler did not mention, is little is being done to build a similar infrastructure bringing work to the public, an obligatory step in the process of translational research.

Moving research from an experimental or basic clinical setting to the final ideal outcome of public policy, where people directly receive the benefit of the research is complex and staggering to the imagination. This complexity, although evident and apparently no less important in industrialized countries such as the United States, is even more challenging in developing countries where barriers to this process are often beyond the control of the most knowledgeable public servants.

The aforementioned movement has been known as "translational research", a term frequently mentioned but poorly understood by academics, researchers and health care professionals. This lack of understanding promotes insignificant impediments in the very process

that seeks to ensure that new treatments and research knowledge actually reaches the patients and populations for whom these were intended.

In the past several years, various institutes have given generous funding to America's best physician-scientists in an effort to make full use of new opportunities in translational research. In a similar manner, the NIH expects to fund several centers of translational research (TR) with a budget of \$500 million per year by 2012 (Travis, 2007). However, such ongoing programs continue under intense scrutiny, raising doubts on whether the research being funded is truly translational or simply a continuation to the already extended support to hundreds of investigators interested in human disease research.

What is Translational Research?

Before trying to define the word "Translational Research" (TR), it is most appropriate to define the word "Translate". According to the Merriam-Webster Dictionary the word translate is "to turn into one's own or another language". The Oxford English Dictionary defines it as "expressing the sense of words or text in another language or converting into another form or medium. In the context of translating research into practice, translation can therefore be understood as the process that converts a highly research-based language to a more understandable and commonly one used by those who conduct interventions or by the public. Several brave attempts to define TR have been made. One early attempt is found in Louis Pasteur's documented feeling when writing "To an individual who devotes his or her life to science, nothing can give more happiness than when the results immediately find practical application". He then concluded: "There are not two sciences. There is a science and the application of science and these two are linked as the fruit is to the tree".

In more recent years others have continued these attempts: “TR is the application of a discovery to the practice of Medicine (Hait, 2005); “The effective translation of the new knowledge, mechanisms, and techniques generated by advances in basic science into new approaches for prevention, diagnosis, and treatment of disease is essential for improving health (Fontanarosa & DeAngelis, 2002); “Moving from evidenced based medicine to sustainable solutions for public health problems (Lean, Mann, Hoek, Elliot, & Schofield, 2008); “The application of findings derived in basic science to the development of new understanding of disease mechanisms, diagnoses, and therapeutics in humans” (Nathan, 2002).

When gathering all these definitions, there is a common ground to the use of the word “Translational Research”. That is, to refer to processes and steps needed to ensure effective and widespread use of science –based programs, practices and policies or translational knowledge- to bridge the gap between the research and policy-making communities.

To clarify the concept of TR, the Institute of Medicine’s Clinical Research Roundtable in 2003 described two” translational blocks” in the clinical research enterprise labeled as T1 and T2. T1 was described as” the transfer of new understandings of disease mechanisms gained in laboratory into the development of new methods for diagnosis, therapy, and prevention and their first testing in humans” and T2 as “the transition of results from clinical studies into everyday clinical practice and health decision making” (Sung, Crowley, Gene, & al, 2003). Before recognizing the implications that each block has in TR, it is pertinent to emphasize they are two distinct processes with goals, setting, study designs and investigators that differ. In this manner, T1 research requires mastery of molecular biology, genetics and other basic sciences. It requires appropriately trained clinical scientist working in strong laboratories with cutting edge technologies; and a supportive infrastructure within the institution.

In contrast, T2 research is a community and ambulatory care setting where population-based interventions and practice-based research networks bring the T1 research to the public. It requires mastery of the “implementation science” of fielding” and evaluating interventions in real-world settings and of the disciplines that inform the design of those interventions, such as clinical epidemiology, communication theory, behavior science, public policy, financing, organizational theory, system design, informatics and mixed method/ qualitative research. A third block (T3) incorporates research processes to evaluate the complex interacting environmental and policy measures that affect susceptibility to disease and sustainability of clinical and public health strategies. Therefore, practitioners, policymakers and the public need sound evidence from different and new methods, involving both experimental and non-experimental methodologies, sensitive to cultural and ethnic priorities.

If dividing the process into blocks facilitates understanding the complexity of TR, it would also be useful in bringing out the deficiencies and gaps that can help to clarify the confusion between the basic discoveries - to- Intervention development types of research and the development-to-delivery research ones. One such deficiency is that T1 attracts more attention and funding then T2 as seen in NIH higher budgets for basic research when compared to health services research budgets in the last decade (Moses, Dorsey, Matheson, & Their, 2005) (NIH, 2007). In addition, the Agency for Healthcare Research and Quality (AHRQ) whose ultimate goal is T2 research translation (making sure that AHRQ research findings are widely disseminated and ready to use in everyday health care decision making) allocates \$300 million per year, representing just over 1 % of the NIH budget (AHRQ, 2001). Thus, in the United States, T1 seems to profoundly overshadowed T2. Moreover, until recently, T2 translation was not recognized as part of the translational process and was not included in its definition.

An important but somewhat controversial implication of this two-phase process, especially in what relates to how resources and attention are distributed among them, lies on the assumption T2 could save more lives than T1. Even though T1 projects occasionally yield breakthroughs that visibly improve the disease prognosis, they may do less to decrease morbidity and mortality than T2 projects. If the health care system performed better in delivering existing treatments than in producing new ones, speculation would support far greater benefit for patients with T2 enterprises (Lenfant, 2003b)

Lastly, much of the confusion about the differences in purpose and methods of the two phases of the translational process relates to confusion about the differences in purpose mentioned above and methods of efficacy versus effectiveness studies. Efficacy is defined as the tested impact of an intervention under highly controlled circumstances. Clinical efficacy studies more appropriately designated “clinical research” is T₁ or block one translational process. Such studies maximize internal validity, that is, the degree to which one can conclude with confidence that the intervention caused the result. On the other hand, effectiveness is the tested impact of an intervention under real-world circumstances. These studies maximize external validity, that is, the degree to which one can generalize from the test to other time, places, or populations (Glasgow, Lichtenstein, & Marcus, 2003).

Difference between Research and Policymaking

Many efforts are currently made to assure that research is used in policy decisions and to bring researchers and policymakers closer together. Bringing the research and policy world together is not a small or insignificant task. Difficulties in doing so originate from the vast differences separating them. While research is methodical, carefully planned and rigorously

designed to avoid outside influences, policy-making is unpredictable and often influenced by external events (special interest groups, among other factors). In addition, research runs in long timeframes compared with the fast-pace mode seen in policymaking. Thus, several questions remain to be answered. How can we make sure that research findings are an integral part of the policymaking process? How can we prevent negative attitudes towards research exhibited in recent years? What can be done to build policy makers' capacity to use research? Are the results from clinical trials and demonstration-research projects likely to be applied in a practical clinical setting? In other words, how can we bridge the gap between research and policymaking communities?

Identifying the potential user of research and policymaking

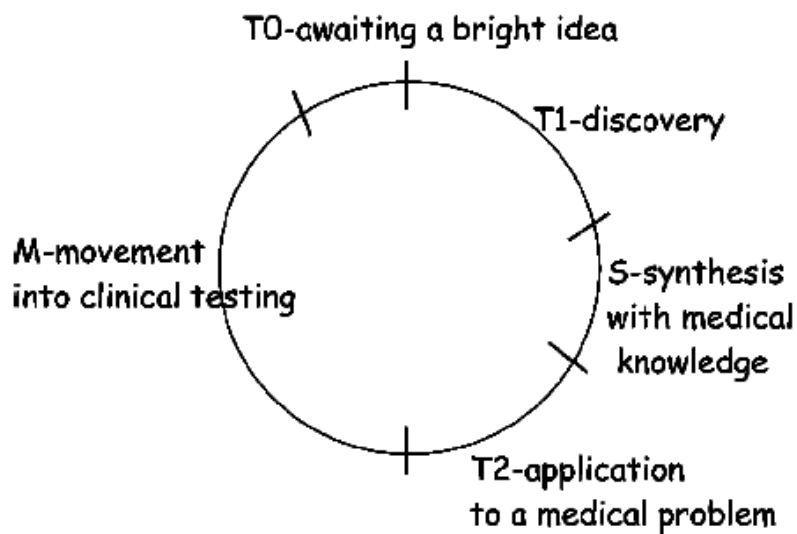
As an initial step in the process to ensure effective and widespread use of translational knowledge to bridge the gap between the research and policy-making communities, it is important to identify the full range of outside users of research evidence (not within the research community itself). These include the general public, patients, health professionals, healthcare managers, biomedical company executives and public policymakers. It also includes intermediary groups such as the media, civil society groups, professionals associations and other groups that work in the interface between researchers and users of research evidence such as those who produce research evidence. The public policy side includes elected officials, their political advisors and civil servants. Professionals engaged in continuing education of health professionals should give special attention to policymakers' as it is they who will often try to change health policy to facilitate learning and behavioral change that are their main objectives,

who will try to change continuing education policy and last who will try to change health policy to the benefit of their patients.

Understanding the Translational Research cycle

Academic centers in contrast to biotechnology and pharmaceutical industry have more difficulty participating effectively in the process of TR possibly because the academic center are not structured to participate in TR. Understanding how the TR cycle works can be the next step in closing the well established gap and is helpful in uncovering barriers present in each stage. As well described (Hait, 2005), the TR cycles shows the interaction of research users in each stage while pointing out the barriers or checkpoints that can obstruct the performance of the cycle. Before illustrating the important features of the cycle, it is relevant to mention the lack of an important stage in the TR cycle, the dissemination (activities that lead to the point of adopting an intervention and placing it into practice) and implementation stage (where research finding or evidence-based strategies are put into practice at the level of individual, organization, community, and policy), pivotal in completing the translational process.

At the T_0 resting phase, generation of a great idea and formulation of that idea into a testable hypothesis is required. It is then followed by the T_1 testing phase where the great idea is subjected to interrogation through scientific inquiry. This later stage implies forming research teams where students, postdoctoral fellows and more established scientists in order to interact. The checkpoint generated between the great idea and the discovery is the T_0 / T_1 checkpoint where barriers include lack of creativity, methodology, innovation, skill, funds, space, and the ability to form an effective team.



The translational research cycle. Adapted from Hait W, 2005

Next, the synthesis phase (S) requires potentially important information of a discovery be placed in front of people who understand the scientific basis of medicine and are familiar with the clinical problem. The T_1 / S checkpoint is the barrier between the new discovery and understanding its importance to clinical medicine. Cultural differences between scientists and clinicians set the stage for its components, which include lack of a properly trained workforce, lack of appropriate venues for interdisciplinary discussions, and academic disincentives to participation in team research. It is crucial in order to bypass this barrier that clinicians are able to understand the methodologies and significance of laboratory finding and scientist gain interest in understanding human biology and pathology.

The T_2 application phase requires the ability of researchers to determine the importance of a discovery to human biology. At this stage the access to predictive animal models, human tissue and body fluids as well as pathologist, pharmacologist, surgeons, biostatisticians among

other specialist, is most critical. It is followed by the movement phase (M) where preclinical studies enter the clinic, complicating the process with the participation of a more expanded team (physicians, nurses, research coordinators, lawyers, experts in informatics, regulatory experts and many others).

Lastly, the T₂ / M checkpoint is the most intimidating of all checkpoints. Its components include the lack of role models, mentors, models of human disease, access to human tissues, funding, and powerful tools for conducting research with human subjects and evaluating interventions (e.g., innovative trial design, screening procedures, etc.). It requires knowledge of policies and procedures regulating the conduct of research on human subjects and the ability to overcome obstacles to material transfer and intellectual property rights. It implies the need to overcome obstacles such as FDA, Institutional Review Board, Protocol Review and Monitoring System and Health Insurance Portability and Accountability Act regulations, intellectual property discussions and the practical scientific needs of toxicology and manufacturing.

A Framework to Translational Research

In the translational research process, the “capacity for change”, especially in what regards to primary care practices willingness and motivation to adopt and implement evidence –based care, is a fundamental aspect to consider and needs to be incorporated in a framework that provides guidance for accelerating its use and thus maximizing the efficacy of public health activities. When trying to understand and make sense of the complexities involved in such a process, a basic structure or framework where research and practice activities of translation can be placed is valuable for focusing attention and resources, to where they might have the greatest

impact while identifying areas of activity that are still underdeveloped. In addition, such a framework can help maximize collaborations among researchers, practitioners, and our public health partners to increase the use of evidence-based interventions, and increase dialogue to refine or redefine the roles of researchers and public health practitioners.

To initiate the construction of such a framework, the Centers for Disease Control and Prevention (CDC) proposed a large-scale systematic plan by identifying fundamental elements of the overall life of an intervention so practitioners from multiple disciplines could maximize the return on investments from translation initiatives and increase the use of evidence-based interventions to promote health and disease prevention strategies (Wilson & Fridinger, 2008). It is mainly an aid for identifying key points of interface between and among public health researchers, practitioners, and others where decisions are made about adopting and using an intervention.

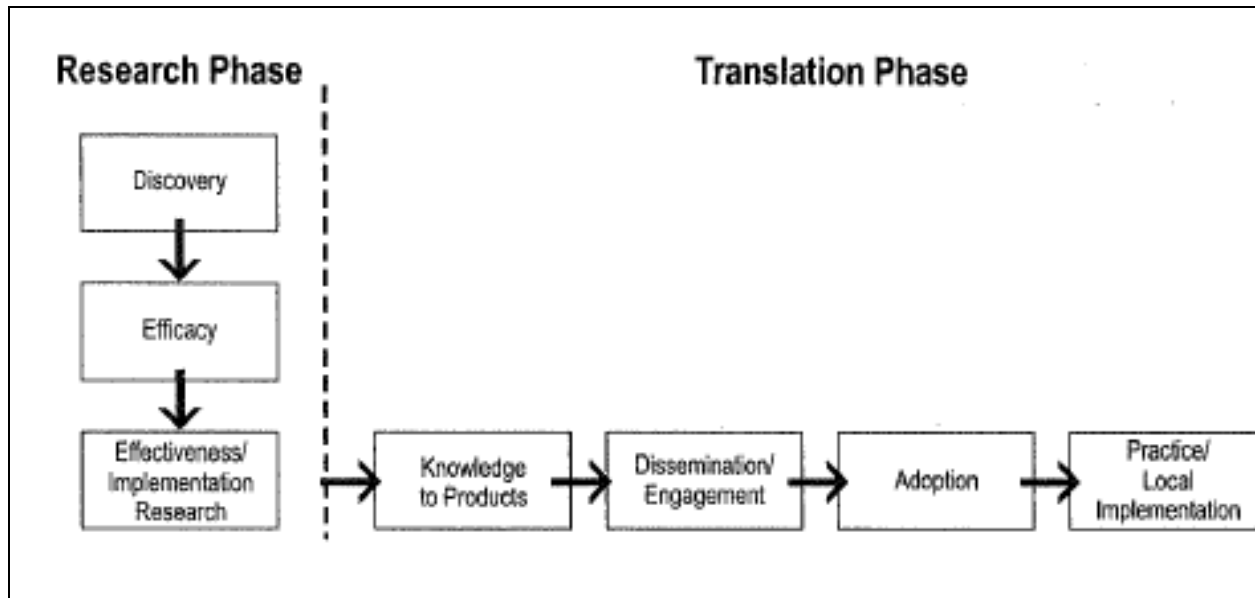
The CDC work group identified three main phases during the life stages of an intervention: research, translation and institutionalization. This last, was not the focus of their initial work. The research phase included: discovery, efficacy and effectiveness. The latter two have been previously defined; however, within effectiveness research is implementation research. Implementation research was defined as the study of local implementation that involved the practitioner together with the student, employee, client, patient or service user in a joint decision-making process that involves simultaneous consideration of evidence, professional values, political considerations, and individualized goals (Sanderson, 2003). All these considerations can also eventually constitute barriers to the translational process and will be addressed later.

In the translation phase, dissemination, adoption, and practice were included.

Dissemination is the targeted and facilitated process of distributing information and materials to organizations and individuals who can use them to improve health. Diffusion was distinguished from dissemination as a passive process rather than a purposeful, targeted, and facilitated process (Flay, et al., 2005). The activities carried out in dissemination include engaging those who decide which interventions are adopted and which are discontinued. It includes the active participation and collaboration of stakeholders who can mobilize resources and influence systems to change policies, programs, and practices. Dissemination activities lead to the point of adoption to put an intervention into practice. Past the point of adoption the next includes applying knowledge and skills in the implementation of the intervention. A more focused part of practice is local implementation, in which research findings or evidence-based strategies are put into practice at the level of individual, organization, community, and policy. In between the research and the translational phase, a transition box known as “knowledge to products” was added to include information necessary to enable practitioners to use other intervention formats like guidelines, checklists, and policies for the different existing stakeholders.

The CDC report has therefore given an important insight to this process. Other important strategies and lessons learned can be summarized as follow:

- Apart from the effect of the manual format for intervention on the translational process, other intervention formats such as guidelines; checklist, policies and mass-mediated interventions must be translated. In other words, additional packaging may be required to enable practitioners to use them effectively. This can be done through a complete understanding of the end-users, such as public, press, patient, provider, policymaker, or private sector organization.



The research and translation phases of an intervention. Adapted from Wilson and Fridinger, 2008.

- Other key processes in translation such as feedback loops, evaluation, and supporting structure must be added to the above-mentioned scheme in order for it to function well.
- That the whole life of an intervention is not linear. That is, it requires feedback loops and these are likely to be numerous and iterative. For example, in order to improve public health practice, a critical feedback loop is from practitioners to developers of the evidence-based intervention (EBI). I would add, equally important, is the feedback from the developer of the EBI to the practitioner and to other stakeholders such as legislators

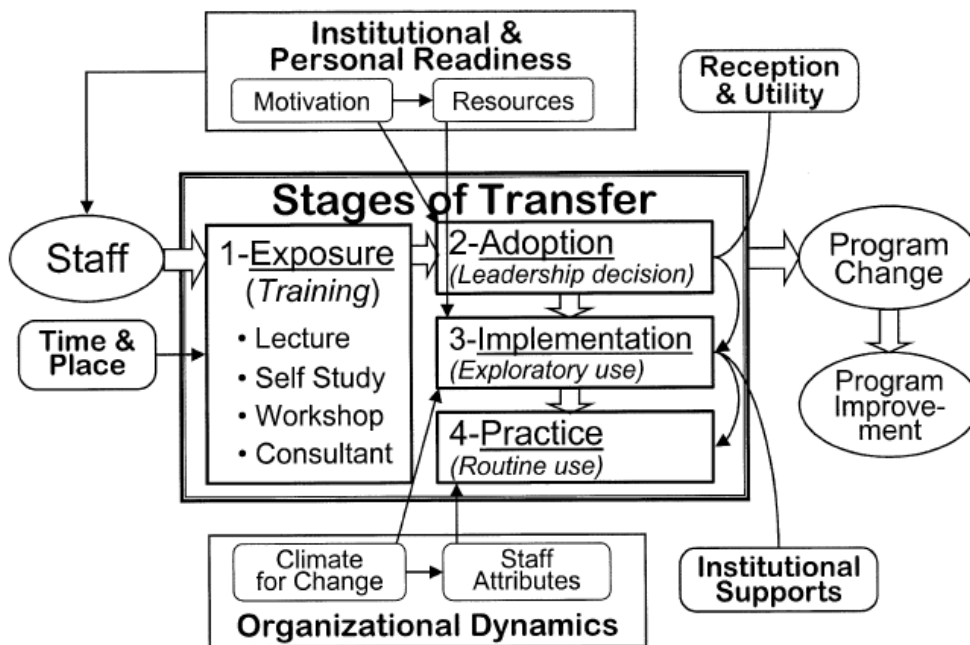
and policymakers. For example, in the process of passing a bill, it is necessary to have the expertise of the person who developed the intervention present and who is convinced of the benefits of the intervention, in order to explain to the politicians, who normally does not understand the scientific language and has no hands-on experience with the issue, in a manner that will help the advocacy process and lead to adoption of the intervention.

- Essential to the mentioned organizational framework is the use of appropriate marketing techniques to adapt, package and disseminate effectively tailored interventions to various targeted audiences and practice setting in a way that decisions to adopt and implement are enhanced and if possible, institutionalized or make it part of a culture/practice.

In using marketing to enhance the adoption and implementation of evidence-based strategies it is most useful to follow Maibach et al recommendations by (1) conducting consumer research with prospective adopters to assess how implementation of evidence-based strategies enhances their organization's mission, (2) building sustainable distribution channels over time, and (3) improving access to easily implemented evidence-based programs (Maibach, Van Duyn, & Bloodgood, 2006).

As mentioned before, the capacity to change is a fundamental aspect to consider when translating research into practice and implies influential factors that also need to be incorporated into a framework that provides guidance for accelerating its use and thus, maximizing the efficacy of public health activities. This model called "The Program Change Model" (Simpson, 2002), incorporates theoretical contributions and industry research finding from the field of organizational behavior and includes influential factors, some similar and others complementary, to those proposed by the CDC framework mentioned above. It includes four stages: exposure,

adoption, Implementation, and practice.



Program change model for transferring research to practice. Adapted from Simpson DD

Briefly, stage one (exposure), claims the need of adequate readiness for change as indicated by motivation (perceived need for change and pressure for change) from both program leaders and staff members as well as sufficient institutional resources (facilities, equipment, training and staff) in order for innovation to be adopted (second stage). Adoption of new techniques or procedures can be through individual decisions guided by reception and utility of innovation or through group decision necessary when attaining general program goals. Stage three (implementation), facilitates the decision process to adopt an innovation. It includes factors such as: climate for change (staff cohesion, communication, openness to change, clarity of mission and goals and others), institutional support that encourages and sustains innovation through monitoring, feedback and the provision of formal and informal rewards that reinforce

positive program change. Lastly, whether a new innovation is incorporated into standard clinical practice largely depends on staff attributes (professional growth, efficacy, adaptability etc.) to promote the change process. It is worthy to mention that all the aforementioned factors may serve as barriers to the process.

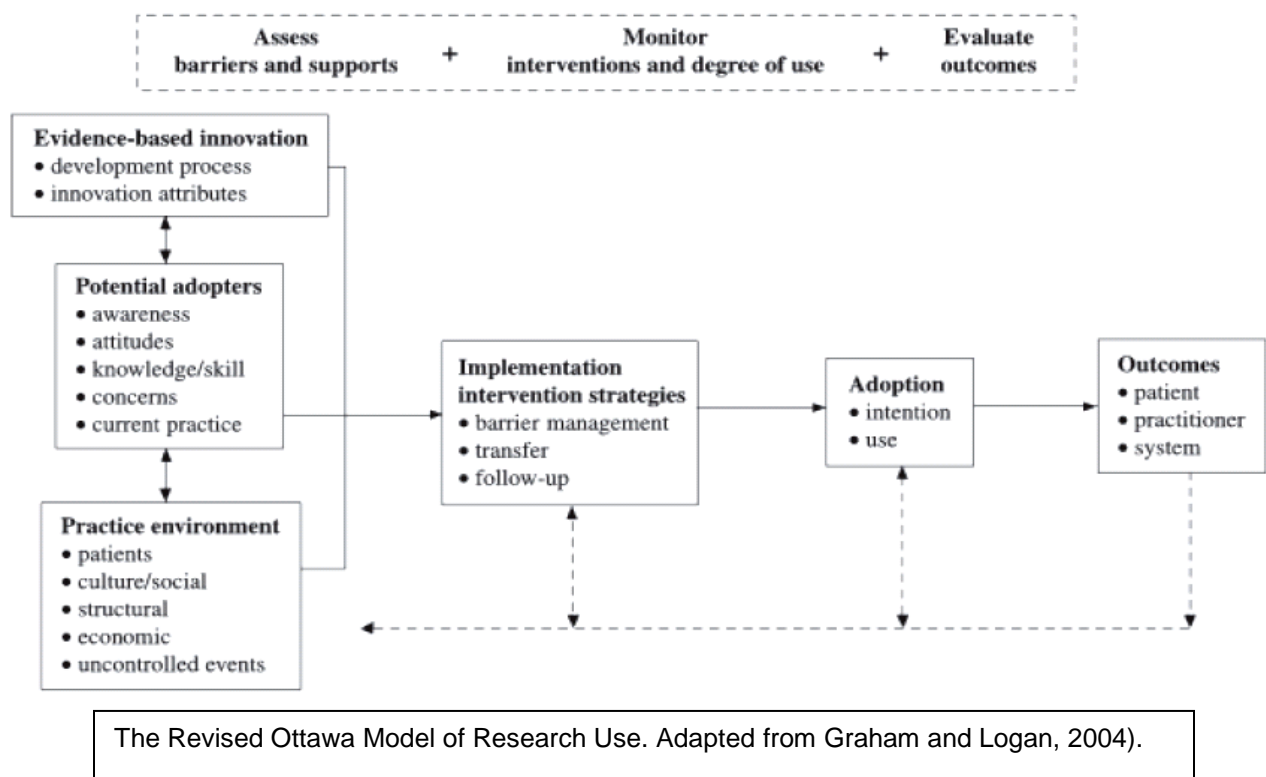
Knowledge translation: Bridging the Know - Do Gap

Knowledge translation plays a prominent part in bridging the research and policy-making communities with an end-goal that seeks to move knowledge, usually research findings, from one community to another (Lavis, 2006). It is by far, the most challenging opportunity for public health in the current century to strengthen aspects of the health system such as equitable access and coverage, health information systems, and human resources. Most importantly, knowledge translation is a non linear, cross-cutting process that involves not only knowledge from research findings, as mentioned above, but also knowledge created from the dynamic interaction of people who unite to resolve public health problems, to learn from each other and ultimately, to promote productive change. In addition, from the moment knowledge is generated to its application is known to be a complex process influenced by factors that include local context (where practices take place) and the perceived relevance of knowledge (how the public and other users of knowledge perceive the evidence of research).

In October of 2005 the World Health Organization (WHO) in collaboration with the Canadian Coalition for Global Health research defined Knowledge Translation as “The synthesis, exchange, and application of knowledge by relevant stakeholders to accelerate the benefits of global and local innovation in strengthening health systems and improving people’s health” (WHO, 2007). In addition, to show the relevance of this process, the WHO has

established a Knowledge Management and Sharing department with a vision for “global health equity through better knowledge management and sharing (WHO, 2005). This initiative seeks to bridge the know-do gap by ensuring that people have the right information at the right time and by facilitating the application of that information into policy and practice, ensuring that research is put into action and that training of new researchers in KT concepts is accomplished.

One of the primary challenges facing these initiatives is to plan and determine the most effective strategies to promote the use and application of research. For this to happen, a more robust framework that provides direction for planning and guiding knowledge translation activities is necessary.



The Ottawa Model of Research Use (OMRU) developed by Logan and Graham provides a useful framework to assess, monitor and evaluate knowledge translation strategies based on identified barriers and supports to research use (INCLIN, 2005). These strategies have been

developed mainly in industrialized countries and continue to be developed with the intention of promoting the utilization of evidence and knowledge by policymakers, health care professional and the public. Its use in developing countries is yet to happen or in desperate need of its application. The model is based on the principle that the most efficient way of applying research evidence is by tailoring KT strategies to the leading barriers and supports found in a particular setting. Thus, identifying these barriers and supporting elements while modifying them into a unique setting is crucial. Once again, this process is neither linear nor sequential (although the graphic illustrated below is presented as linear and sequential) but dynamic with a set of interactions and exchanges among involved researchers, users and stakeholders taking place not necessarily in a specific order or time.

As mentioned, the first key element of this model is the assessment of barriers and supports categorized into three levels:

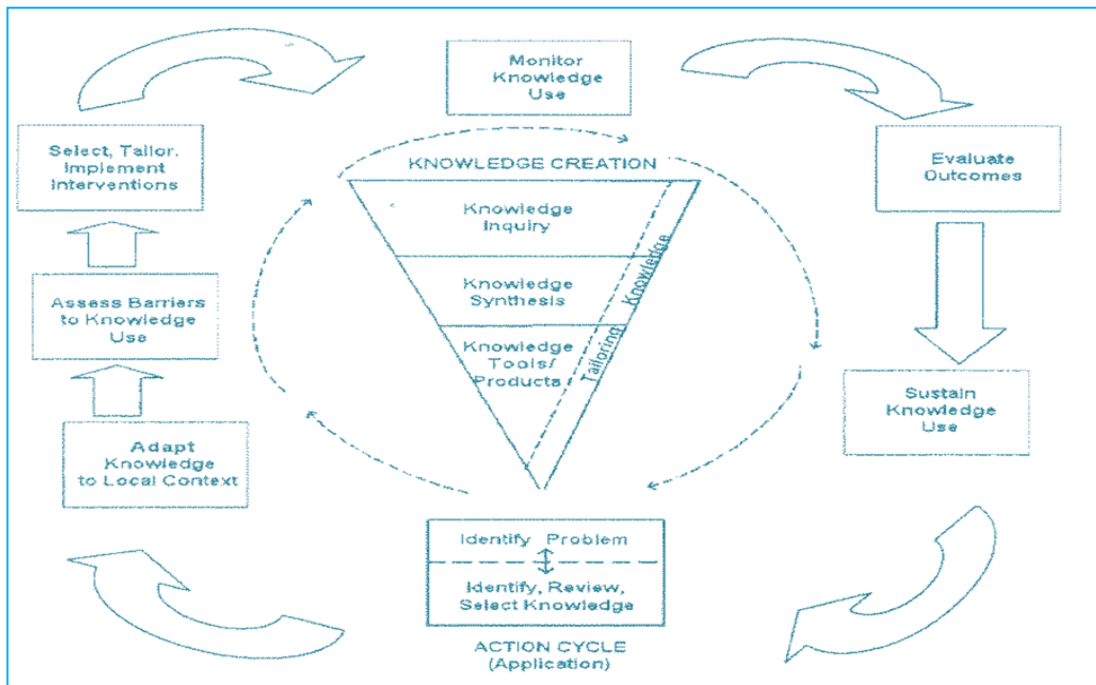
- A. The structural, social, patient, and economical influences within the practice and policy environment. It is important to emphasize that for an effective intervention to be delivered there needs to be minimal human resources, financing, supply systems and drugs available. Such is the case in developing countries where financial resources are scarce. In addition, the application of research can be hampered when the political environment is corrupt and unstable.
- B. The attitudes, knowledge, motivation and skills of potential adopter or target users. In this regard, potential users may just not have the knowledge of the research evidence or their behaviors may be based on ideologies, culture or preconceived beliefs instead of evidence. Incentives to change behavior as well as strategies to address these beliefs must be developed.

C. The perception of the research evidence and innovation by the public and other users.

Here, the difficulty in applying the evidence and the negative feelings about the validity and credibility of the evidence may delay its application.

Once the knowledge translation strategy has been tailored and executed, assessment on whether the research has been applied and has resulted in improved health comes is necessary. One widely used resource for this purpose is from The Cochrane Collaboration Review Group on Effective Practice and Organization of Care, which developed specific methods for synthesizing, finding, and analyzing the evidence on what KT strategies work in order to change or improve the behavior of health care professionals and ensure knowledge is adequately applied. Therefore, assessing and then addressing the beliefs and perceptions of health care professionals is crucial before implementing an intervention to change practice.

Finally, measuring and monitoring the use of the research and the resulting health outcomes of KT strategies is vital to the process. As stated by Santesso et al, strategies to ensure knowledge is used or translated into policy, practice and improved health is highly variable and dependent on the setting and success hinges on whether the strategies have been tailored (Santesso & Tugwell, 2006). Therefore, in order for an intervention to be translated into practice it must be demonstrated to be effective in a real-world clinical setting in the community or targeted to a patient population that is commonly seen in such setting.



Knowledge to action process model. Adapted from Graham et al.

The above framework “Translation-to-action” is a most appropriate response to the growing awareness that research findings are not making their way into practice with a current emphasis on evidence-based, cost-effective, and accountable health care. The illustration is one of the ways of minimizing the gap of what has been described as the knowledge –to-action gap, using a more generic terms such as action, to replace the word practice with the intention of including the use knowledge by practitioners, patients, policymakers and the public. It emphasizes on the exchange of knowledge between relevant stakeholders that result in action and the need to cultivate these relationships (Graham, et al., 2006).

Some plausible causes of the know-do gap	Some ongoing efforts to address the causes
Limited access to information, technology and medicines (digital divide, IP rights, patents)	Medline, Health InterNetwork Access to Research Initiative (HINARI), Health information network (HifNet), Iowa University, Global Health Library, specialized libraries & portals (Maternal and Child Health (MCH), AIDS), Google scholar, virtual health libraries and other country initiatives, Digital Solidarity Fund
Ignorance of evidence-based problem solving and learning approaches in health (including lack of learning from development projects due to structure of aid process)	International Network of Clinical Epidemiology (INCLIN), Cochrane collaboration, Cambell collaboration, Guidelines and courses by professional associations, Health Evidence Network-like networks, etc.
Lack of need-driven research, particularly in developing countries	National Institutes of Health (country priorities), Council on Health Research for Development (COHRED), Global Forum for Health Research (GFHR), WHO Special Programme on Research and Tropical Diseases (TDR), specialized initiatives, including new Public Private Partnerships in Research & Development for diseases of poverty
Lack of ownership of knowledge by potential "users"/"adopters"	Successful immunization campaigns, tobacco-free initiatives, social entrepreneurship, knowledge brokering (Canada, Netherlands)
Lack of creation/exploitation of knowledge from practice (evaluation, continuous improvement)	Institute for Health Care Improvement (IHI), Bangladesh Rehabilitation Assistance Committee (BRAC), Management Sciences for Health (MSH), Tanzania Essential Health Interventions Project (TEHIP)
Slow diffusion of innovation or scale up	Strategic advocacy (Medecins Sans Frontier), social marketing (Greenstar-Pakistan-based social marketing organization), social entrepreneurship (BRAC)

Some Causes of the Know-do gap and ongoing efforts to address them. Adapted from (Pablos-Mendez & Shademani, 2006).

Barriers to translational research

Up to now, several general and specific barriers to the translational process have been mentioned in the illustrated models. However, other relevant barriers are not well recognized and need to be addressed in order for effective translation to happen. It is important to acknowledge that the inability to remove such barriers has a tremendous impact on the ability of health professionals to provide safe, effective patient care and to reduce the cost of health care delivery (McGlynn, Asch, Adams, & al., 2003).

One important barrier worthy of mention is that created from the complexity, volume, scope and nature of information needed to deliver patient and population-based care. Efforts in the biomedical informatics area (electronic medical record systems) have attempted to tackle this barrier (Clayton, Narus, Huff, & al., 2003), but unfortunately have not been widely adopted and their potential has not been recognized world-wide. Furthermore, information technology (IT) has been applied to every phase of the clinical research venture and its use has demonstrated benefits in many areas including initial study design, data collection and analysis, and study monitoring (Payne, Johnson, Starren, Tilson, & Dowdy, 2005). However, current isolated data entry systems and databases are insufficient and research-specific systems are rarely integrated with clinical IT systems or with other research systems. Hence, these systems have experienced less than the desired adoption by physician-investigators, mainly because of factors such as the absence of required infrastructure components (systems and standards for the exchange of data between unequal systems and aggregation for population-based research), end-user acceptance and training in the use of computer systems, and policy-based opposition concerning the adoption of new Information technologies (Kukafka, Johnson, Linfante, & Allegrante, 2003).

An important number of applications have been developed for the translational research field but are yet to be appreciated. They range from the rapid use of preclinical studies, to the multicenter transferring of clinical protocol documents, to their execution integrated into the clinical or community context and their subsequent analysis and dissemination. It is then clear that significant improvements in those applications, their integration, and national standards will be required in a near future and that efforts must

be undertaken in policy, education, and funding to ensure that physician-investigators have quick access to appropriate information technologies.

Another important barrier to the translational process and the adoption of health interventions is the lack of cost-effective studies crucial when considering the enormous increase in health care cost (calculated to be approximately \$2.26 trillion in 2007, and driven by the use of medical technology) (NHE, 2009). Economic evaluation is vital in providing data to inform efficient allocation of resources and control costs in any health care setting by facilitating a systematic approach when assessing the benefits of specific health interventions relative to their cost. Cost-effectiveness analysis is the most commonly use approach for economic evaluation in health care. Unfortunately many interventions are poorly assessed for cost-effectiveness prior to use, limiting their access to the public policy level.

As mentioned before, public policy barriers are equally important and systematic reviews suggest that knowledge translation process targeted at public policy makers should involve interactions between researchers and public policymakers and timely response to public policymakers' queries (Lavis, 2006). Other key public policy barriers identified (Aspden, 2002) are:

- Reimbursement policies not friendly to innovation or other interventions.
- Inability of federal agencies to cope in the face of a significant increase in the amount and a broadening in the scope of medical innovations
- Excessive regulation inhibiting change and costly to implement (for example, The Centers for Medicare and Medicare Services (CMS) have 130.000 pages of rules, regulations, and guidelines).

- Public policy changes and the difficulty in anticipating its impact are a major uncertainty for business enterprises.
- Older Policies may no longer provide the right incentives

Practice Environment

- structural (e.g. health systems)
- interest group pressure or peer pressure on decision makers
- insufficient economic/budget resources and/or time to include research in decision making
- centralisation of power and information, or hierarchy of power
- political instability and high turnover
- lack of access to research, data and analysis
- culture not conducive to evidence based decision making
- censorship and control

Potential Adopters

- generation of decision making based on past experiences
- local or indigenous knowledge
- variation in incentives and motivations to change
- lack of communication and contact with researchers
- negative feelings about research and its use
- lack of awareness about relevant research
- lack of skills to apply and use research

Perception of Evidence

- lack of timely or relevant research
- politicisation of research
- poor quality of research
- credible evidence
- inaccessible or useful format

Barriers and Supports to Knowledge translation. Adapted from Santesso et al 2006
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What needs to be done to move research to public policy?

Through the reviewed literature, one can conclude that we are still in the developmental stage of the process that will ensure that good, sound, reliable knowledge is translated into the hands of the public. It is clear that much needs to be done. Although it is true we need more effective treatments, we must stop regarding clinical science and the ecological support from effective policies as independent disciplines. In addition, we must also control for unfairness in funding and publication to reflect a more integrated view of what research is necessary. This

would imply that doctors must already make evidence based treatment decisions and monitor their outcomes, and politicians and policy makers need to access best quality evidence and show how it informs the development of policies. It also means that the translational process does not end when research findings are published and better communication between - researchers and practitioners, practitioners and policymakers, researchers and policymakers- is fundamental for public outreach. Training in translational research methods for clinicians, guideline writers, grant awarding bodies, and policy makers will enable better assessment of complex evidence bases, help to integrate effective and culturally sensitive interventions with supporting environmental changes, and encourage continuous improvement of evidence based public policies.

It is also clear that an agreed upon conceptual frameworks and learning platforms to spread good practices are urgently needed, as well as the availability of funding, accountability, and evaluation systems. As well expressed by Hiss, barriers are not universal in their effect on all science, nor are they universal in their ability to impair adoption by all potential recipients. Therefore, the role of TR is to analyze the influence they have in particular situations and the development of specific strategies to deal with these situations (Hiss, 2001).

Lessons Learned

Many Lessons have been learned so far from the literature to help us understand what needs to be done to move the process in the right direction, that is, towards public policy practices. Some lesson are summarize below:

- Knowledge translation is about turning knowledge into action and includes the processes of both knowledge creation and knowledge application
- Healthcare professional need to learn about planned-action theories and frameworks so as to be able to understand and influence change in their practice setting

- Knowledge translation includes and build on continuing education and continuing professional development
- Continuing education should apply strategies shown to be effective at transferring knowledge
- Continuing education should be based on the best available knowledge whether in the form of knowledge tools (e.g., practice guidelines), knowledge synthesis (e.g., literature reviews) or by primary knowledge inquiries.
- System lack an environment that promotes incentives, rewards systems, to encourage and enhance sharing, learning and applying and reapplying knowledge for problem solving
- Research and public policy making are often distinct and asynchronous processes
- Knowledge-translation processes offer the potential to build bridges between research and public policymaking process
- Effective strategies to ensure knowledge is translated into policy are highly variable and dependent on the setting and success depends entirely on whether the strategies have been tailored.
- The importance of using research in health decision making at the individual and population level has been increasing recognized by developed countries and low- and middle-income countries
- Increase the number of systematic reviews to address the questions asked by public policy makers through participation the Cochrane Effective Practice and Organization of Care Group.

- Lead meeting between researchers and policy makers to identify what challenges policymakers expect to face in the future and what kind of research needs to be funded now to address those challenges

Recommendations to overcome future challenges and barriers (IDRC, 2003)

- strengthen links between researchers and decision makers to create long standing relationships and long term commitment
- improve communication by training policy makers and researchers: assist researchers to communicate their findings to policy makers in an understandable and stimulating way, and sensitize policy makers about the usefulness of research results as an input for decision making
- create positive attitude towards the use of research findings
- reduce mutual mistrust
- promote better understanding of policy making by researchers and researchers by policy-makers
- promote understanding of researchers of timely, relevant questions to policymakers and policy makers about how to obtain valid answers to these questions
- work together to set priorities
- create a knowledge warehouse of the pool of knowledge and review and synthesize research
- provide incentives for researchers to produce usable research and for policymakers to pay attention to it
- disseminate information and facilitate its use

- consider knowledge brokering
- train policy makers to commission, interpret and put research into practice
- encourage researchers to respond to demand and produce research that is operational and practical
- increase the credibility of researchers in developing countries

❖ **Applying Knowledge Translation to a Neonatal Program: Initial steps**

Issue that needs to be address and literature review

To increase the likelihood that our intervention would be transferred into a policy, there was a need to incorporate a framework that provided guidance for accelerating its use and thus maximizing the efficacy of public health activities. The following action-plan adapted from Graham et al (knowledge to action process model) was applied:

- Identify a problem that needs addressing
- Identify, review, and select the knowledge or research relevant to the problem (e.g., practice guidelines or research findings)
- Adapt the identified knowledge or research to the local context
- Assess barriers to using the knowledge
- Select, tailor, and implement interventions to promote the use of knowledge (i.e., implement the change)
- Monitor knowledge use
- Evaluate the outcomes of using the knowledge
- Sustain ongoing knowledge use

In the case of Colombia, by utilizing the knowledge to action process model we identified the need for NCPAP to be transferred to the clinical practice as part of a policy change. We identified and reviewed the knowledge and began the process of adapting the identified knowledge to the local context. The following is the summary of these initial steps.

When looking at the most prestigious reports on Respiratory Distress Syndrome (RDS) of the premature, such as those from the World Health Organization (WHO), the Lancet neonatal survival series and the Bellagio series, there is no reference included in the neonatal package that addresses the proposed intervention for the treatment of RDS in the premature newborn. Current recommendations are limited to oxygen administration through nasal cannula that in the majority of cases is insufficient to support infants with RDS. This certainly gains enormous significance when reviewing the literature for the impact of none-treated or poorly treated illnesses, such as the one addressed in the program we are now relating to. First, the fact that 4 million babies die each year in the first month of life, corresponding to 40% of the total child mortality worldwide (Lawn, Cousens, & Zupan, 2005), is worrisome. Of these deaths, 3 million happen in the first week of life. Preterm babies (less than 37 weeks gestational age) comprise 24% of all deaths and a large proportion of these infants die from respiratory failure secondary to RDS.

Globally, of the total infant deaths during the first month of life, 99% occur in low and middle income countries. Unfortunately, research aimed at increasing survival of this population has been directed to the 1% of neonatal deaths in high income countries (Darmstadt et al, 2003: Lawn et al 2005). Availability of mechanical ventilation (MV), an expensive intervention proven to increase survival of infants with respiratory failure, is very limited in developing countries. The previous has led to the search for interventions that are cost-effective with the potential to impact infant survival.

In Colombia, the country selected to develop a model for international collaborative research that inspired this project, the infant mortality rate is 19.5 deaths per 1000 live births and the neonatal mortality rate is 13 deaths per 1000 live births. Compared to the United States who ranked 34th with an infant mortality rate of 6.3 deaths per 1000 live births in the table of countries with the lowest infant mortality rates, Colombia ranked 111th (O'Connor, 2008) (CIAWF).

Based on the research developed in Colombia that demonstrated a significant decrease in the need for mechanical ventilation with the use of NCPAP with and without very early surfactant in premature infants with RDS, the current project was designed to transfer this knowledge into public health policy. This intervention would be introduced in all levels of care (I, II, and III) and would be used as the initial therapy for stabilization and management of premature infants who show clinical evidence of RDS at the time of delivery. In support of the use of NCPAP, multiple studies conducted in different countries have shown similar results to the Colombia NCPAP trial (9-12). A recent study from Australia (The COIN study) comparing NCPAP without surfactant to mechanical ventilation with surfactant in premature infants with RDS, demonstrated a significant decrease (59%) in the need for MV in infants exposed to NCPAP and no additional increase in chronic lung disease and mortality (Morley, et al., 2008). A meta-analysis by the Cochrane Collaboration reviewed evidence from six randomized clinical trials indicating that infants with RDS treated with early surfactant replacement therapy and NCPAP were less likely to need mechanical ventilation, less likely to develop pulmonary complications, and less likely to suffer from air leak syndrome (Stevens, Blennow, Myers, & Soll, 2008). Addition of early surfactant to NCPAP in the Colombia NCPAP trial showed a higher reduction in the need for MV (29%) compared to exposure to NCPAP without surfactant

(39%). A significant reduction in air-leak syndrome was also observed. Put into context both the COIN study and the Colombian CPAP trial demonstrate that NCPAP with and without surfactant are effective strategies to reduce the need for MV and possibly prevent the development of chronic lung disease. In countries with limited resources for healthcare, the use of NCPAP has the potential to decrease infant and neonatal mortality.

Once the research relevant to the problem was identified, reviewed and selected, it was imperative to adapt the identified research to the local context, that is, the process that individuals or groups go through as they take decisions about the value, usefulness and appropriateness of a particular knowledge to the setting as well as the activities that will customize the knowledge to a particular situation. Learning more about Colombia's health system, specifically Colombia's health care reform (Law 100/1993) was necessary in order to adapt the identified research to the local context and have an understanding of the barriers and interactions needed to overcome them and move the process forward (Rosa & Alberto, 2004). Although a country of hard working people, wonderful traditions, and incredible human and natural resources, it is important to say that the Colombian economy is characterized by unequal distribution of income, a high degree of informality and a temporary nature of employment. In spite of this, Colombia spends 9.3% of its GDP in health (Fedesalud). Its efforts to achieve universal health insurance through its reform (contributory and subsidized regimens) has not been successful and on the contrary has generated opposition, mainly because the system relies on the market intermediation of EPSs (health promoting entities) and ARSs (managers of the subsidized Regimen), creating problems associated with high transaction cost, inefficient management, and slow-moving flow of resources. Moreover, the financial sustainability of the system is threatened by problems related to the Country's economic crisis, fiscal evasion,

corruption in the management of subsidized regimen and inaccurate economic forecast on which the expansion of coverage has been based. Hence, regardless of some improvements, at least 4 million inhabitants of the non-poor strata lack coverage for health care (Ruiz, Amaya, & Venegas, 2007).

As in other developing countries, Colombia is known to have a limited capacity for research, a major obstacle towards obtaining relevant evidenced-based knowledge to address major health care problems. Limited financial support (e.g., grant), a deficit of locally trained researchers, limited time for academic research and poor quality research infrastructure are some of the factors that explain this limited capacity. Moreover, in Colombia, government grant support is limited by budget restrictions and high competition from excessive amount of medical graduates as well as red tape, which discourage many researches to apply for them.

Identification of barriers within Colombia is a necessary step in planning the transfer of knowledge to clinical practice and the community. The development of the Colombian Neonatal Research Network and the subsequent conduct of randomized controlled trials directed at obtaining relevant knowledge to the health care needs of the neonatal population in this country have been obligatory steps in overcoming some of these barriers by building research capacity. The proposed neonatal project represents transfer of knowledge from T1 to T2 and subsequently to T3. Dissemination of knowledge was addressed through different venues. Cultural barriers were identified in planning and executing this phase of the project in order to promote awareness and implementation of the knowledge. For this purpose, information was tailored to target stakeholders through the distribution of published evidence based literature, both in English and in Spanish peer reviewed journals and books, power point presentations for national and local medical meetings, the media, and letters with relevant information to physicians, public health

care workers and government and state officials. More importantly, this program seeks to continuously cultivate relationships with different stakeholders and have available a follow-up process to ensure that such information is received and response is obtained within an acceptable timeframe. In several occasions information was sent more than once and personal phone-calls were made to assure contact information had not been changed or that targeted stakeholders had not placed this information in the back of their busy agenda. Multiple internet live conferences facilitated the process between researchers and stakeholders specifically members of the Colombian Neonatal Research Network (Rojas, Lozano, Rojas, & CNRN, 2007). A personalized cover letter was designed that would catch the reader's attention and was mailed together with a copy of the Colombian CPAP trial publication in Pediatrics. An additional strategy was to send a power point presentation with a summary of our program, in addition to personalized letters and electronic mails with the intention of encouraging recipients to read the information. Respected high circulating newspapers ("El Tiempo" and "El Espectador") and magazines have been selected to help propagate and incite awareness of the project ("Semana", "Times", "Si...Si Colombia", "Cambio", "Cromos"). Programmed national and local medical meetings and face-to-face visits with government and state officials will help to ensure that our information is adequately delivered and that later in the process, our intervention has led to a change in medical practice and government policy.

A strategy we selected to move the political process was to work through the Colombian Neonatal Association, which would serve as a "Policy Promoter" responsible for moving policy through its developmental stage and at the same time serve as a target to other stakeholders. We then focused on other interest groups both inside and outside of the government and analyzed their influence, authority, status, resources and skills. Some identified stakeholders included:

- ⊙ Colombian Neonatal Association
- ⊙ Medical Community in Colombia
- ⊙ Maternal Child Health Program in Colombia
- ⊙ News media including national Newspapers and radio
- ⊙ Health care policymakers within the Ministry of Social protection and Legislators
- ⊙ Health Care Administrative Services: entities that promote health (EPS), and institutions that provide health care services (IPS)
- ⊙ Regional Government health departments in Colombia

In favor of our project and to the success of the policy efforts is the relatively low political cost to other stakeholders, mainly because our intervention would be implemented in a setting where no or very minimal technology is available and infant and neonatal mortality is high. The proposed intervention would give employment, reduce government, state and municipal cost, and most importantly, reduce the economical and emotional burden to families of premature infants within the targeted communities.

When looking at the environmental conditions, we did research on the political climate including a list of people in current health-related government positions, changes in party alliances and agenda. To have access to them it was occasionally necessary to make social contact through colleagues, friends and family. Although familiar with the social and economic conditions through recent visits to the country, we interviewed with different people of different social classes to gain perception of expectations, public opinion and changes in demographics, inflation, economic growth and unemployment. Because one of our main objectives is to introduce the proposed intervention in all levels of care (I, II, and III), an understanding of the

level of education and motivation of the available workforce that would carry out the intervention is planned as a vital activity within this project (e.g., physicians, nurses, transportation personnel from care levels I and II to level III centers) (Koyamaibole, Kado, Qovu, Colquhoun, & Duke, 2006). To this aim, power presentations on the subject have also been conducted in urban and rural areas of Colombia.

Lastly, we are in the process of obtaining financial support for a cost-effectiveness analysis of our intervention in order to obtain buy-in from all stake holders including physicians, hospital administrators and politicians (Adam, et al., 2005). Concurrently with the dissemination and implementation phase of our project we will develop evaluation instrument to determine the impact this intervention has within our target population in Colombia. We expect that the results of this project will serve as a model for other developing countries and that developed countries like the United States will adapt this technology to decrease morbidity and the cost of health care, a relevant issue for all countries.

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